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# Application of Central Corneal Thickness for the Diagnosis of Canine Glaucoma

## 개의 녹내장 진단 시 중심각막두께의 적용

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## ABSTRACT

Glaucoma is second most disease causing vision loss in dogs. Retinal ganglion cell death caused by elevated intraocular pressure (IOP) and it leading to irreversible vision loss in dogs and humans. Early detection and regularly monitoring of glaucomatous dog is essential to maintain vision for a long time. Currently, detection and monitoring of glaucoma mainly rely on measurement of IOP by tonometers in dogs. Since introduction of the ultrasonic pachymeter, correlation between central corneal thickness (CCT) and glaucoma is widely investigated in humans. CCT is known to the most potent predictor of conversion of ocular hypertension into glaucoma in the Ocular Hypertension Treatment Study. Although, central and peripheral thickness of the cornea was already investigated,

there has been little attention for correlation between glaucoma and CCT in dogs. Therefore, the purpose of the present study was to evaluate the possibilities of CCT for diagnosis and monitoring of glaucoma in dogs. This study consists of two chapters.

Chapter I demonstrated the effect of CCT on IOP measurement by tonometers in normal dogs. Both eyes of 60 normal beagles dogs were used in this study. After ophthalmic examinations of both eyes, IOP was measured by the TonoVet, followed by the TonoPen XL in half of the dogs and the other half were applied reverse order. All CCT measurements were performed 10 minutes after the use of the second tonometer. There was a correlation between IOP values obtained by the two tonometers and CCT readings in regression analysis (TonoVet : $p = 0.002$, TonoPen XL : $p = 0.035$). The regression equation demonstrated that for every 100 ㎛ in CCT results in 1 and 2 mmHg elevation of IOP as measured by the TonoPen XL and the TonoVet, respectively.

Chapter II evaluated changes in CCT according to experimental adjustment of intraocular pressure (IOP) in canine eyes. Both eyes of 25 clinically normal beagle dogs were used in this study. To adjust and measure IOP, each eye was cannulated with two 26-gauge needles under inhalant anesthesia. One needle was connected to a pressure transducer, and the other was connected to an adjustable bag of physiologic saline. IOP was stepwise increased from 10 mmHg to 70 mmHg in 10 mmHg increments (Group T). Also, IOP was maintained at 15 mmHg (Group C15), 30 mmHg (Group C30), 45 mmHg (Group C45), 60 mmHg (Group C60) and 75 mmHg (Group C75) during the experiment. CCT was measured with an ultrasonic pachymeter every 10 minutes after cannulation. According to increased IOP, the CCT showed an initial decrease and then an increase after passing the lowest point.

Based on the results of the present studies, effect of CCT should be considered in IOP measurement with tonometers in dogs. Also, CCT itself changed with an increased IOP, exhibiting an initial decrease and then a subsequent increase in dogs. Therefore, it is suggested that CCT could serve a factor for diagnosis and monitoring of canine glaucoma.

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**Keywords: central corneal thickness, intraocular pressure, glaucoma, tonometer, dog**

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# CONTENTS

**CHAPTER II.**

**Acute Changes in Central Corneal Thickness According to Experimental Adjustment of Intraocular Pressure in Normal Canine Eyes**

# GENERAL INTRODUCTION

The glaucomas are a diverse group of diseases united only by the fact that intraocular pressure (IOP) is too high to permit the optic nerve and, in some species, the retina to function normally (Miller, 2008). Progression of glaucoma divided into five stages. (a) an initial event usually involving the aqueous humor drainage pathway, (b) physical changes causing aqueous humor outflow obstruction, (c) elevated IOP that is too high for normal optic nerve axoplasmic flow and blood flow, (d) retinal ganglion cell (RGC) dysfunction with resulting optic nerve degeneration and atrophy, and (e) visual-field loss and blindness (Gelatt *et al.*, 2007). Because, irreversible blindness occurs in final stage of glaucomas, early detection and monitoring of glaucoma is essential to maintain vision.

Visual field testing is critical in the clinical diagnosis and monitoring of glaucoma in humans (Heijl, 2011). However, there are no reliable visual field tests for management of canine glaucoma. Instead of visual field tests, measurement of IOP with tonometers is currently main way for diagnosis and monitoring of glaucoma in dogs (Miller, 2008). Recently, ophthalmic diagnostic equipments such as high-resolution ultrasonography, ultrasound biomicroscopy, optical coherence tomography, pattern and flash electroretinography, visual evoked potential and ultrasonic pachymeter have been investigated to apply for diagnosis and monitoring of glaucoma in humans and dogs (Bentley *et al.*, 2003; Gibson *et al.*, 1998; Manni *et al.*, 2008).

Among them, the ultrasonic pachymeter has a noninvasive, simple method and high degree of interobserver reproducibility in humans (Miglior *et al.*, 2004). Since the introduction of the ultrasonic pachymeter, CCT has been investigated in human glaucoma patients. CCT can be a responsible factor for inaccuracies of tonometric values, because

tonometers estimates IOP through the cornea. Potential underestimation of the true IOP in subjects with thinner CCT can disrupt proper treatment for glaucoma in humans. Also, independent of the influence on tonometric values, thinner CCT itself can be a risk factor for development of glaucoma in humans. Possible correlation between CCT and the optic nerve head glaucomatous damage is able to influence the risk of developing glaucoma or progression of the disease (Manni *et al.*, 2008).

This study was designed to investigate possibility of CCT as a diagnosis and monitoring of canine glaucoma. First, effect of CCT on widely used two tonometers (TonoPen XL and TonoVet) in veterinary medicine were determine and compare in normal laboratory beagle dogs (Chapter I). Second, CCT acute response to the experimental adjustment of IOP was investigated to identify possibility of CCT for monitoring of glaucoma (Chapter II).

# CHAPTER I.

## Effect of Central Corneal Thickness on Intraocular Pressure with the Rebound Tonometer and the Applanation Tonometer in Normal Dogs

## Abstract

To evaluate the effect of central corneal thickness (CCT) on the measurement of intraocular pressure (IOP) with the rebound (TonoVet) and applanation (TonoPen XL) tonometers in beagle dogs. Both eyes of 60 clinically normal dogs were used. The IOP was measured by the TonoVet, followed by the TonoPen XL in half of the dogs, while the other half was measured in the reverse order. All CCT measurements were performed 10 mins after the use of the second tonometer. The mean IOP value measured by the TonoVet (16.9 ± 3.7 mmHg) was significantly higher than the TonoPen XL (11.6 ± 2.7 mmHg; $p < 0.001$). The IOP values obtained by both tonometers were correlated in the regression analysis ($\gamma^2 = 0.4393$, $p < 0.001$). Bland-Altman analysis showed that the lower and upper limits of agreement between the two devices were -0.1 and +10.8 mmHg, respectively. The mean CCT was 549.7 ± 51.0 microns. There was a correlation between the IOP values obtained by the two tonometers and CCT readings in the regression analysis (TonoVet: $p = 0.002$, TonoPen XL: $p = 0.035$). The regression equation demonstrated that for every 100 microns increase in CCT, there was an elevation of 1 and 2 mmHg in IOP measured by the TonoPen XL and TonoVet, respectively. The IOP obtained by the TonoVet and TonoPen XL would be affected by variations in the CCT. Therefore, the CCT should be considered when interpreting IOP values measured by tonometers in dogs.

# Introduction

The intraocular pressure (IOP) is formed due to a balance between the production and drainage of the aqueous humor (Gum *et al.*, 2007). Accurate measurement of IOP is essential for diagnosis, treatment, and monitoring of various ophthalmic diseases, particularly glaucoma (Gelatt *et al.*, 2007). A manometer can be used to precisely and directly measure IOP. However, this method is not appropriate in clinics because it is invasive and requires general anesthesia. On the other hand, tonometers which are clinically available make use of various principles to indirectly measure IOP using the cornea. Unfortunately, indirect measurements through the cornea can give rise to errors in IOP values (Chihara, 2008)

Using the Imbert-Fick law (pressure = force/area) as its basic principle, the applanation tonometer (TonoPen XL), measures the force necessary to flatten a predetermined area of the corneal surface (Goldmann and Schmidt, 1957). Therefore, estimated IOP values will likely be dependent upon corneal surface conditions, such as the central corneal thickness (Goldmann and Schmidt, 1957), the corneal curvature (Harada *et al.*, 2008), and the precorneal tear film (Zeng *et al.*, 2008). Nearly all human studies have shown that the CCT is positively correlated with IOP. However, the effects of other corneal factors are still in dispute (Broman *et al.*, 2007; Kohlhaas *et al.*, 2006; Whitacre and Stein, 1993). The degree that the CCT affects IOP nevertheless varies between each study and tonometer (Bhan *et al.*, 2002; Ehlers *et al.*, 1975; Ileiv *et al.*,2006).

A recently introduced portable tonometer, the rebound tonometer (TonoVet), has also been used to measure IOP in animals (Gorig *et al.*, 2006; Knollinger *et al.*, 2005; Leiva *et*

*al.*, 2006). To measure IOP, this tonometer uses a return-bounce motion and a microprocessor to analyze the deceleration of the probe after its impact with the cornea (Kniestedt *et al.*, 2008). Previous human studies have shown that the rebound motion of the probe is also affected by the same corneal surface conditions as mentioned above (Ileiv *et al.*, 2006; Sahin *et al.*, 2008).

Since the TonoPen XL and the TonoVet are portable and easy to use, they are useful for measuring IOP in animals (Gelatt *et al.*, 2007). Although the TonoPen XL and the TonoVet have been evaluated for dogs in previous studies, the CTT was not evaluated in these studies (Gorig *et al.*, 2006; Knollinger *et al.*, 2005; Priehs *et al.*, 1990; Rusanen and Kontiola, 2004). Up until now, CCT values have only been used to evaluate endothelial toxicity caused by phacoemulsification (Lynch and Brinkis, 2006), intraocular drugs (Gerding *et al.*, 1990) and laser photocoagulation (Chandler *et al.*, 2003) in dogs, but also can be used for assessing the toxicity of topically applied drugs. Hence, the purpose of this study was to determine and compare the effect of CCT on IOP values obtained by two different tonometers, the TonoPen XL and the TonoVet, in normal beagle dogs. In addition, we determined if there were an agreement and a correlation between IOP as measured by the two tonometers in dogs.

# Materials and Methods

## 1. Experimental animals

Both eyes of 60 clinically normal beagle dogs (28 females and 32 males) were used in this study. Mean body weight was 8.5 kg (5.4 ~ 12.4). All animal procedures were performed in accordance with the guidelines of the Institutional Animal Care and Use Committee of Seoul National University. Eye examinations were performed with the Schirmer tear test (STT, Schirmer Tear Test, Schering-Plough Animal Health, New Jersy, USA), an indirect ophthalmoscope (Vantage, Keeler Instruments Inc., Broomall, Pennsylvania, USA) with a 30-diopter condensing lens (Volk, Volk optical inc., Ohio, USA) and a slit-lamp biomicroscope (SL-202, Shin-Nippon, Tokyo, Japan). Dogs with lower than 10 mm wetting/min of STT values were excluded to remove the effects of abnormal precorneal tear film on IOP measurements (Zeng *et al.*, 2008).

## 2. Experimental design

All procedures were performed between 4 ~ 8 PM in order to minimize the effect of diurnal variations on the IOP (Gelatt *et al.*, 1981; Greller *et al.*, 2008). The first examiner (TH Kim) conducted all CCT and IOP measurements, while the second examiner (YW Park) noted the data separately. To reduce observer bias, the first examiner was masked to the values during the experiment. The first eye was selected randomly, from thereon after, the second eye was assessed. All measurements, including the CCT and IOP, were performed using the central cornea, while the dog was sitting in a comfortable position.

IOP was recorded 3 times with each tonometer and the mean value was used for the present study. An average of six successive readings were recorded with the rebound tonometer (TonoVet, Tiolat, Helsinki, Finland) and four successive readings were recorded with the applanation tonometer (TonoPen XL, Mentor, Norwell, USA). If the standard deviation (SD) of the estimated IOP was greater than normal (TonoVet, d was blinking or an error sign ["-"] was displayed; TonoPen XL, over 5 % error bar), the value was discarded. The CCT was measured once in each eye by an ultrasonic pachymeter (PACHMATE DGH 55, DGH Technology Inc., Pennsylvania, USA). The pachymeter displayed an average ± SD of 25 successive readings. If the SD of a measurement was greater than 10 microns, the value was also discarded.

The dogs were divided into two even groups in order to avoid examination order error. (group 1, 18 females and 12 males; group 2, 10 females and 20 males). The protocol for group 1 began with the measurement of IOP by the

TonoVet. Then, 1 drop of proparacaine (Alcaine, Alcon, Puurs, Belgium) was applied to the cornea twice at intervals of 1 minute. One minute after the application of proparacaine, IOP was measured by the TonoPen XL. After 10 minutes, the CCT was measured by the ultrasonic pachymeter.

In group 2, 1 drop of proparacaine was first applied to the cornea twice at intervals of 1 minute. One minute afterwards, IOP was measured by the TonoPen XL. Three minutes later, IOP was measured again by the TonoVet. The CCT was then measured by the ultrasonic pachymeter 10 minutes after the last IOP measurement by the TonoVet.

## 3. Statistical analyses

Data from the two tonometers and the pachymeter were analyzed using SPSS 12.0 (SPSS Inc., Illinois, USA). The level of significance used was $p < 0.05$. The mean of IOP, difference in IOP (TonoVet minus TonoPen XL), and CCT values were then calculated. Using the paired t-test, the mean IOP values were compared in order to determine the difference between the two tonometers. The difference in IOP values based on gender (female and male), inter-group (1 and 2), and inter-eye (right and left) were compared using the Student's t-test. Simple linear regression analysis was utilized to determine the correlation between IOP and CCT values and was also used to determine a correlation between the CCT and the difference in IOP. The correlation and agreement between IOP values measured by the TonoVet and the TonoPen XL were analyzed with the simple linear regression and Bland-Altman analysis. For the Bland-Altman analysis, the MedCalc 10.4.8 program (MedCalc software, Mariakerke, Belgium) was used.

# Results

## 1. The correlation between IOP and CCT

No statistical differences were observed between the right and left eyes in the CCT and IOP values. As a result, data from both eyes were considered to be independent samples ($p > 0.05$). The mean IOP values ± SD measured by the TonoVet and the TonoPen XL were 16.9 ± 3.7 mmHg (range of mean value of 3 measurements : 8.3 ~ 26.7) and 11.6 ± 2.7 mmHg (range of mean value of 3 measurements : 5.7 ~ 18.7), respectively. The mean difference in IOP was 5.3 ± 2.8 mmHg (-1.0 ~ 16.0) and the mean CCT ± SD was 549.7 ± 51.0 microns (377.0 ~ 657.0) (Table 1). Based on the simple linear regression analysis, IOP values from both tonometers were significantly correlated with the CCT values; more so with the TonoVet than the TonoPen XL (TonoVet, $\gamma^2 = 0.0792$, $p = 0.002$; TonoPen XL, $\gamma^2 = 0.0371$, $p = 0.035$; Fig. 1). The regression equations were y (TonoVet) = 0.020x + 5.790 and y (TonoPen XL) = 0.010x + 5.917, respectively (x = CCT and y = IOP value). In addition, the differences in the IOP were significantly increased with the CCT ($\gamma^2 = 0.0338$, $p = 0.044$; Fig. 2). There was no difference between the mean IOP and CCT measurements by gender. Nevertheless, the mean IOP values of group 1 were significantly higher than that of group 2 in both tonometers (TonoPen XL, p=0.002; TonoVet, p=0.017). Additionally, the mean CCT of group 1 was significantly thicker than that of group 2 ($p = 0.045$).

Table 1. IOP and CCT values of 120 eyes in clinically normal 60 beagle dogs

| Group | No. of eyes | TonoVet (mmHg) | TonoPen XL (mmHg) | Difference in IOP (mmHg) | Mean CCT ± SD (㎛) |
|---|---|---|---|---|---|
| Group 1 | 60 | 17.7 ± 3.4†* | 12.3 ± 2.8†* | 5.4 ± 2.5 | 559.0 ± 41.8* |
| Group 2 | 60 | 16.1 ± 3.8†* | 10.8 ± 2.4†* | 5.3 ± 3.0 | 540.4 ± 57.6* |
| Total | 120 | 16.9 ± 3.7‡ | 11.6 ± 2.7‡ | 5.3 ± 2.8 | 549.7 ± 51.0 |

† Significant difference in IOP between the two tonometers within same groups ($p < 0.001$).

‡ Significant difference in IOP between the two tonometers in 120 eyes ($p < 0.001$).

* Significant difference in CCT and IOP obtained by the same tonometer between groups ($p < 0.05$).

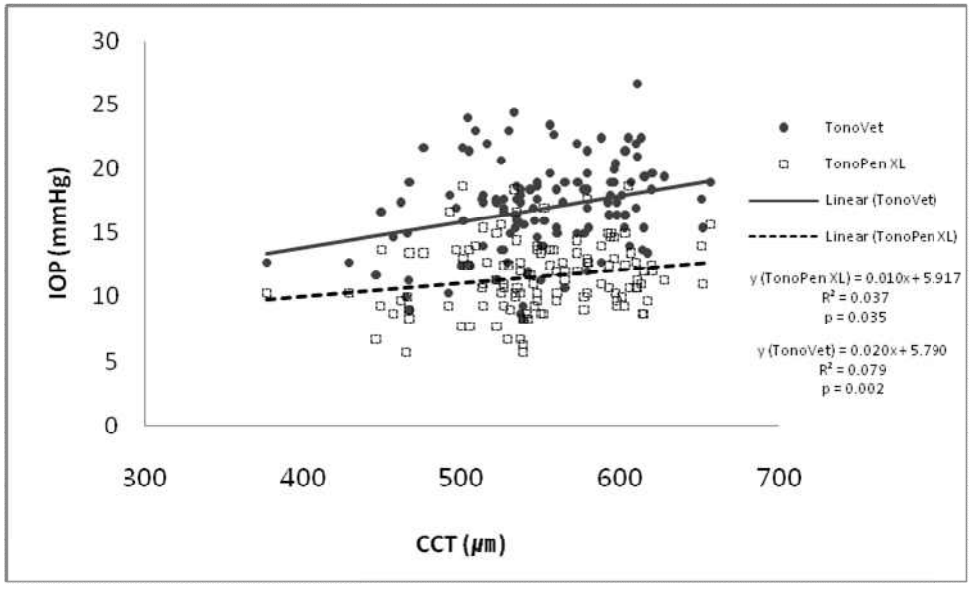


Fig. 1. Scatterplot and linear regression of central corneal thickness (CCT) and intraocular pressure measurements obtained by TonoPen XL (open square, □) and TonoVet (gray circle, ●). The linear regression formula shows that the TonoVet was affected twice as much by CCT than the TonoPen XL.

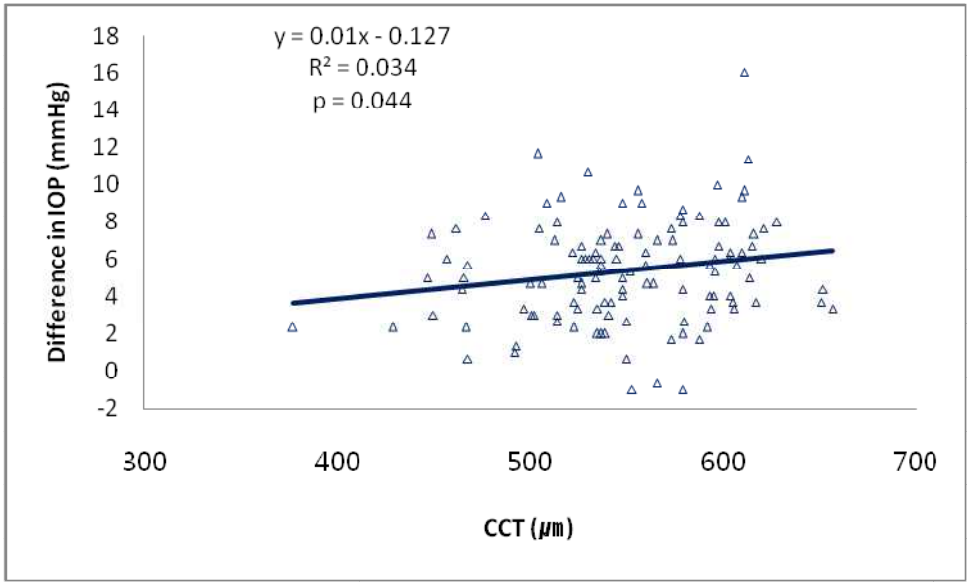


Fig. 2. Scatterplot and linear regression of central corneal thickness (CCT) and the difference of intraocular pressure (IOP) readings between the two tonometers (TonoVet minus TonoPen XL). The difference in IOP increased with thickening of the CCT.

## 2. The correlation and agreement of two tonometers

Based on the paired t-test, the mean IOP values measured by the TonoVet and the TonoPen XL were significantly different ($p < 0.001$; Table 1). On the other hand, the linear regression analysis showed that IOP values obtained by the two tonometers were significantly correlated ($\gamma^2 = 0.4393$, $p < 0.001$; Fig. 3), and most plots (114 eyes) depicted a large distribution between the upper and lower 95% limits of agreement (Fig. 4). Since the estimated IOP values obtained by the TonoVet were greater than those acquired by the TonoPen XL, there was little agreement shown between the two tonometers. The IOP values obtained by the TonoVet were higher than those of the TonoPen XL, except for three eyes. In addition, the 95% limits of agreement between the two devices were -0.1 to 10.8 mmHg based on the Bland-Altman analysis (Fig. 4).

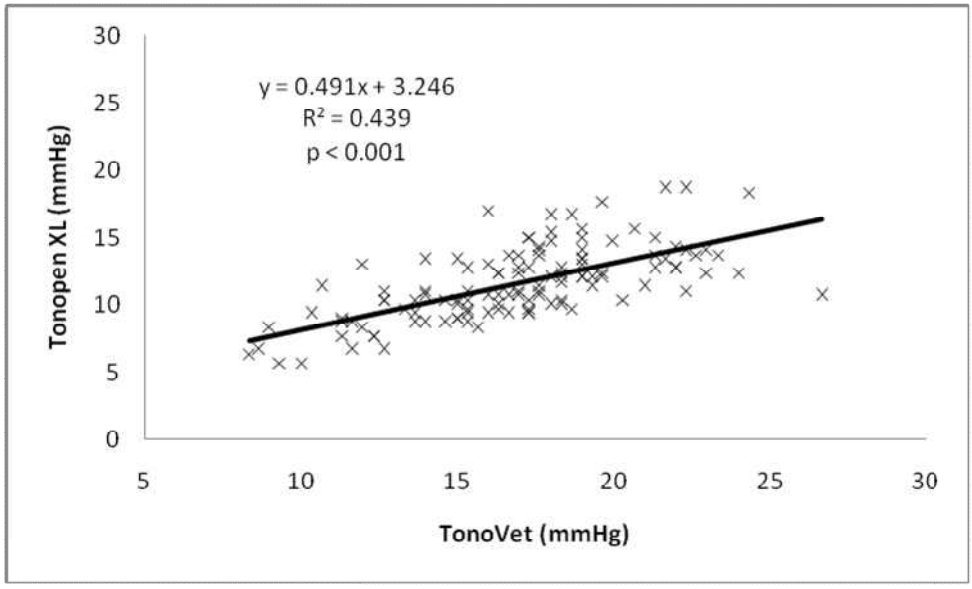


Fig. 3. Correlation between intraocular pressure readings obtained with TonoPen XL and TonoVet.

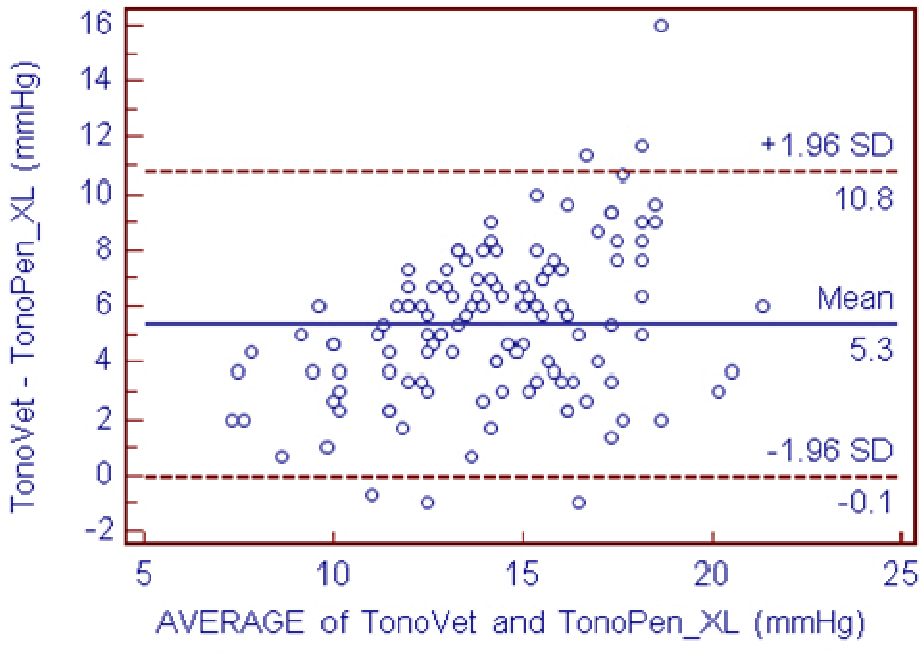


Fig. 4. Bland-Altman plot shows the difference in intraocular pressure (IOP) readings between the TonoVet and the TonoPen XL against the mean IOP values of two tonometers. Estimated IOP values with the TonoVet were greater than that of TonoPen XL; lower and upper limits of agreement between the two tonometers were -0.1 and 10.8 mmHg, respectively. In contrast, the IOP obtained by the two tonometers were correlated; most plots were distributed within 95% limits of agreement.

## Discussion

The results of this study elucidated that the IOP values measured by the tonometers tended to be elevated as the CCT increased. However, the degree of dependency on the CCT was more prominent in the rebound tonometer (TonoVet) than the applanation tonometer (TonoPen XL) in dogs. Despite the correlation between the two tonometric values, IOP measurements obtained by the TonoPen XL were also significantly lower than those of the TonoVet (on average, 5.3 mmHg).

The correlation between the CCT and IOP has been widely investigated in human medicine. For example, Goldmann and Schmidt suggested that the corneal thickness could influence IOP measured by applanation tonometry. Thus in humans, IOP should be adjusted according to the CCT (550 microns; Goldmann and Schmidt, 1957). In addition, human case of abnormal IOP measurement caused by an extremely thickened cornea was reported (Johnson *et al.*, 1978). However, the effects of CCT on IOP measurement has not been investigated in dogs. Thus, we conducted this study and it has shown that the CCT does affect IOP measured by different tonometers; specifically, the rebound tonometer (TonoVet) was affected 2 times more than the applanation tonometer (TonoPen XL; Fig.1). Additionally, the difference in IOP values between both tonometers increased as the CCT increased (Fig. 2).

The slopes of Figure 1 showed that IOP values of the TonoPen XL and the TonoVet increased 1 and 2 mmHg for every 100 microns increase in CCT, respectively. Similar to our results, a human study reported that the rebound tonometer was more affected by CCT values than the applanation tonometer (Sahin *et al.*, 2008). IOP measurements by the I-care (the human version of the rebound tonometer) and the TonoPen XL in children

increased 3.5 and 2.3 mmHg for every 100 microns increase in CCT values, respectively. Other studies has also documented that the rebound tonometer showed a steeper slope than that of the applanation tonometer against CCT values (Ileiv *et al.*, 2006).[11]

Since corneal elasticity allows the indirect measurement of IOP, this property is also probably influenced by corneal thickness (Kniestedt *et al.*, 2008; Pallikaris *et al.*, 2005). In the applanation tonometry, more pressure is needed to flatten a thicker cornea, thus causing a greater increase of estimated IOP in a thickened CCT. Also, the rebound motion is increased with the thickening of the cornea, decreasing the deceleration of the probe. For that reason, the estimated IOP in a thickened cornea is higher than in a normal CCT when measured by the rebound tonometer.

Additionally, our results show that, IOP values measured by the same tonometer could be different because of CCT. Therefore, if the CCT is extremely thickened or thinned, the equations shown in Fig. 1 can be used to estimate true IOP values. This method can furthermore be useful in monitoring glaucomatous canine patients with a CCT in an abnormal range.

If eyes with a thick or thin cornea were used to calibrate tonometers, the real IOP values could be over-or under-estimated. Using an ultrasonic pachymeter, a previous study stated that the mean CCT in dogs was 562 microns (Gilger *et al.*, 1991), while our study presented 549.7 microns as the mean value. Although the CCT is affected by body weight and age (Gilger *et al.*, 2008), the mean CCT in dogs should approximately be 550 microns from both studies. Thus, eyes with a CCT within this range should be used for evaluating tonometers in dogs.

Two different statistical methods (the Bland-Altman and simple linear regression analysis) were applied to analyze the correlation and agreement in IOP values obtained by

the two tonometers. The Bland-Altman analysis shows a scatter diagram of the difference plotted against the averages of two tonometers with 95% limits of agreement (Bland and Altman, 1986; Bunce, 2009). This analysis explains the correlation as well as the agreement of two measuring methods. In our results, IOP values obtained by the two tonometers showed little agreement in the Bland-Altman analysis; the lower limit of agreement between the two devices was -0.1 mmHg and only 3 eyes were distributed under 0 mmHg (Fig. 4). Thus, estimated IOP values obtained by the TonoPen XL were lower than the TonoVet. However, there still was a correlation between the two tonometric values; 6 eyes (5%) were distributed beyond the 95% limits of agreement in the Bland-Altman plot. In addition, the simple linear regression analysis showed that IOP values measured by the TonoVet were significantly correlated with IOP values obtained by the TonoPen XL ($p < 0.001$).

The TonoVet showed a strong linear relationship with manometry in dogs (Gorig *et al.*, 2006; Knollinger *et al.*, 2005). In contrast, since the TonoPen XL was developed for humans, a calibration curve is required to compensate for the differences in corneal elasticity between humans and dogs (Dziezyc *et al.*, 1992; Miller *et al.*, 1991).[30, 31] In previous studies, IOP values measured by the TonoPen (Model 1, the old version of the Tonopen) and the TonoPen XL underestimated the IOP compared to the manometer in dogs (Gorig *et al.*, 2006; Rusanen and Kontiola, 2004) and various animals (Passaglia *et al.*, 2004). In addition, a previous report claimed that, unlike the TonoVet, the I-Care developed for humans showed IOP values similar to that of the TonoPen XL (Leiva, 2006).

Görig *et al.* (2006) documented that the mean IOP value obtained by the TonoVet was higher than that of the TonoPen XL in conscious and sedated dogs. In addition, in

manometric measurements using enucleated canine eyes, the slopes of the calibration equations were 1.063 and 0.665 in the TonoVet and the TonoPen XL, respectively. This result shows that the difference in IOP values between the two tonometers increased as IOP also increased. Our results furthermore illustrated a similar tendency: the Bland-Altman scatter plots revealed that the difference widened as the average IOP increased (Fig. 4). This tendency is correlated with the CCT as well because the IOP difference increased with the thickening of the CCT (Fig. 2).

## Conclusions

The present result suggests that the CCT is an important factor to be considered in IOP measurement because it is positively correlated with IOP values as measured by tonometers in dogs. Also, the TonoVet was more affected by CCT than the TonoPen XL.

# CHAPTER II.

# Acute Changes in Central Corneal Thickness According to Experimental Adjustment of Intraocular Pressure in Normal Canine Eyes

## Abstract

Central corneal thickness (CCT) can be a promising source of glaucoma monitoring and diagnosis. This study evaluated changes in CCT according to experimental adjustment of intraocular pressure (IOP) in canine eyes. To adjust and measure IOP, each eye was cannulated with two 26-gauge needles under inhalant anesthesia. One needle was connected to a pressure transducer, and the other was connected to an adjustable bag of physiologic saline. IOP was stepwise increased from 10 mmHg to 70 mmHg in 10 mmHg increments (Group T). IOP was maintained at 15 mmHg (Group C15), 30 mmHg (Group C30), 45 mmHg (Group C45), 60 mmHg (Group C60) and 75 mmHg (Group C75) during the experiment. CCT was measured with an ultrasonic pachymeter every 10 minutes after cannulation. There was a significant difference in the effect of time on CCT ($p < 0.001$) and difference in CCT (dCCT; $p < 0.001$) between groups. The CCT of group C15 remained constant during the experiment. However, group T showed an initial decrease and then an increase after passing the lowest point. Group C30 showed decreasing values for 30 minutes, after which the values remained constant. The values in Group C45 showed no changes for 40 minutes and then increased. The values in group C60 showed no change for 20 minutes and then increased. Group C75 showed a steady increase. In conclusion, the CCT showed two core changes according to increased IOP. This study provides essential basic data to enable further investigation into the association of IOP and CCT in dogs.

# Introduction

The canine cornea consists of five layers: the epithelium, basement membrane, stroma, Descemet's membrane and endothelium (Samuelson, 2007). The normal thickness of the canine cornea is approximately 550 microns in the central area, but the peripheral cornea is slightly thicker (Gilger *et al.*, 1991). Both the epithelium and endothelium control corneal hydration, but the endothelium plays a more important role in this task (Riley, 1971). The pump-leak hypothesis is considered the basic model of corneal hydration control. The cornea consists of two sets of receptors. One senses hydration, and the other modulates the activity of the endothelial pump. In addition, a linking system is needed to connect these two receptors (Fischbarg and Maurice, 2004).

Because the corneal endothelium is in direct contact with the aqueous humor, corneal thickness can be altered by conditions affecting the aqueous humor. Inflammation of the aqueous humor inhibits the function of the endothelial pump, leading to corneal edema (Macdonald *et al.*, 1987). Intraocular pressure (IOP) is formed by the production and drainage of aqueous humor, and changes in IOP can also affect corneal thickness (Ytteborg and Dohlman, 1965a; Ytteborg and Dohlman, 1965b). Two possible mechanisms of change in central corneal thickness (CCT) according to IOP can be considered. One is associated with the pump function of the corneal endothelium, which can be impaired when the IOP reaches the critical pressure. The other mechanism is the direct affect of elevated IOP on the mechanical properties of the cornea (Ytteborg and Dohlman, 1965a).

The ultrasonic pachymeter has disadvantages such as false results due to indentation during measurement, the risk of infection by direct contact and inaccuracy due to the

perpendicularity of the probe placement (Kawana *et al.*, 2004; Solomon, 1999). However, the ultrasonic pachymeter is the gold standard for CCT measurement because it has a noninvasive, simple method and high degree of interobserver reproducibility in humans (Miglior *et al.*, 2004). Since the introduction of the ultrasonic pachymeter, CCT has been investigated in human glaucoma patients. Although this issue remains controversial, patients with a thin CCT have shown a high risk for glaucoma (Gordon *et al.*, 2002).

The current study was designed to investigate CCT acute response to the experimental adjustment of IOP in dogs. In addition, the possibility of CCT as a factor for diagnosis and monitoring of canine glaucoma was investigated.

# Materials and Methods

## 1. Experimental animals and preparation

Both eyes of 25 clinically normal beagle dogs were used in this study. All animal procedures were performed in accordance with the guidelines of the Institutional Animal Care and Use Committee of Seoul National University. Complete ophthalmic examinations were performed before the experiment using a rebound tonometer (TonoVet, Tiolat, Helsinki, Finland), Schirmer Tear Test (Schirmer Tear Test, Schering-Plough Animal Health, Kenilworth, NJ, USA), slit-lamp biomicroscope (Topcon SL-D7, Topcon Corp., Tokyo, Japan) and indirect ophthalmoscope (Vantage, Keeler Instruments Inc., Broomall, PA, USA) with a 30-diopter indirect lens (Classic BIO Lens, Volk Optical Inc., Mentor, OH, USA). To investigate changes in CCT according to stepwise increases in IOP compared with a fixed normal IOP, 30 eyes of 15 dogs were used. The remaining eyes were used to investigate changes in CCT according to a fixed increase in IOP (30, 45, 60 and 75 mmHg).

Before induction of anesthesia, atropine eye drops (Ocutropine, Samil, Kyonggi, South Korea), a combination of phenylephrine and tropicamide eye drops (Mydrin-P, Saten Pharmaceutical, Osaka, Japan), a combination of dexamethasone, polymyxin B and neomycin eye drops (Maxitrol, S.A. Alcon-Couvreur N.V., Puurs, Belgium) and flurbiprofen eye drops (Ocufen, Allergan Sales LLC, Waco, TX, USA) were all applied twice to achieve mydriasis and reduce inflammation induced by anterior chamber paracentesis. Acepromazine

0.03 mg/kg (Sedaject, Samwoo Medical, Chungnam, South Korea), cefazoline 30 mg/kg (CKD Cefazolin Inj., Chong Kun Dang, Gyonggi, South Korea) and dexamethasone 0.3 mg/kg (Je Il Dexamethasone Inj., Je Il Pharmaceutical, Daegu, South Korea) were administered intravenously 5 minutes before anesthesia induction using propofol (Provive 1%, Claris Lifesciences, Ahmedabad, India). Anesthesia was maintained with isoflurane (Ifran, Hana Pharm. Co., Ltd., Gyeonggi, South Korea) and oxygen. During anesthesia, ECG, pulse oxymetry, noninvasive blood pressure, end tidal $CO_2$, capnography and temperature (with a digital thermometer) were monitored.

After induction of anesthesia, the dog was laid in a dorsoventral position during the experiment. To induce extraocular muscle akinesia and prevent pain, retrobulbar injection of 2 ml of 2% lidocaine (Je Il lidocaine injection (2%), Je Il Pharmaceutical) was performed with a 23-gauge retrobulbar needle in each eye using the inferior-temporal palpebral technique (Accola *et al.*, 2006). In cases with inadequate extraocular muscle akinesia, a second injection of 1 ml of 2% lidocaine was performed 10 minutes after the first injection. An eye speculum was placed to expose the cornea after induction of extraocular muscle akinesia. The exposed cornea was frequently lubricated with 0.5% sodium carboxymethyl cellulose (Refresh Plus, Allergan Sales LLC) to prevent corneal desiccation during the experiment.

The anterior chamber was entered with two 26-gauge needles through the limbus (2 and 10 o'clock positions) for each eye. Cyanoacrylate glue (3M Vetbond, 3M Animal Care Products, St. Paul, MN, USA) was used to prevent leakage from the entry site after needle insertion. One needle was connected to a

normal saline reservoir containing 5 IU per milliliter of heparin through a polypropylene line. The IOP was adjusted to different levels by changing the reservoir. The other needle was connected to a pressure transducer system for IOP measurement through a polypropylene line and contained normal saline with 5 IU per milliliter of heparin. The system comprised a pressure monitoring kit (Transpac IV Monitoring Kit, ICU Medical, Inc., San Clemente, CA, USA) with a transducer, polyethylene tubes, monitoring cable (Transpac Reusable Cable, Hospira, Inc., Lake Forest, IL, USA) and a monitor (Datex-Ohmeda S/5, Helsinki, Finland) for continuous monitoring of IOP (Fig. 5). The transducer was positioned at eye level. Before each experiment, the transducer was calibrated to a mercury manometer, and a zero balance was set using the manufacturer's instructions.

Triamcinolone 4 mg/kg (Rheudenolone Inj., Kukje Pharma. Ind., Gyeonggi, South Korea) and gentamicin 8 mg/kg (Kukje Gentamicin Inj., Kukje Pharma. Ind.) were injected into the subconjunctiva to reduce inflammation and infection after the experiment. A combination eye drop comprising dexamethasone, polymyxin B and neomycin was then applied 2 times per day for 1 week.

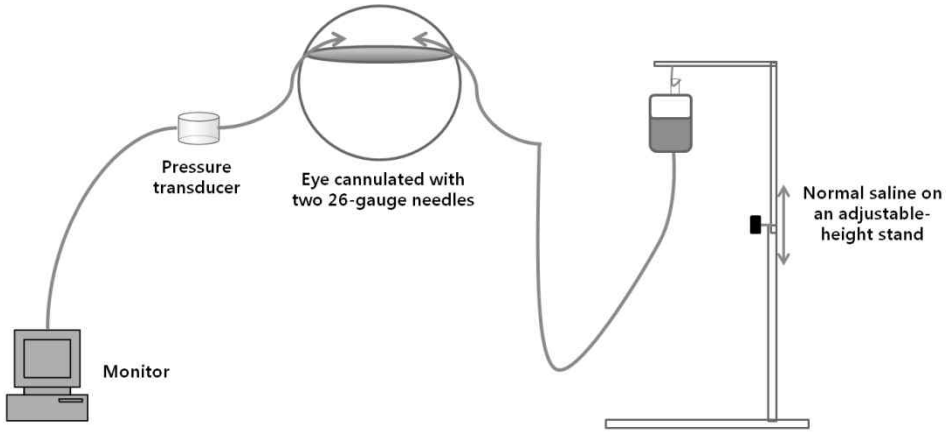


Fig. 5. Schematic of the experiment after cannulation in an eye.

## 2. Procedures for stepwise increase of IOP and fixed normal IOP

Thirty eyes of 15 dogs were randomly assigned to groups T and C15. In group T, the IOP of one eye per dog was adjusted to 10 mmHg immediately after cannulation and was then raised in increments of 10 mmHg until a maximum IOP of 70 mmHg. CCT was measured with an ultrasonic pachymeter (Pachmate DGH 55, DGH Technology, Exton, PA, USA) 3 times at each IOP after each IOP maintenance for 10 minutes. The IOP in the other eye was adjusted to 15 mmHg (group C15) immediately after cannulation, which was maintained throughout the experiment. An ultrasonic pachymeter was also applied every 10 minutes in the same manner as for group T.

### 3. Procedures for fixed increase of IOP

Twenty eyes of 10 dogs were randomly assigned to groups C30, C45, C60 and C75. Each group consisted of 5 eyes from different dogs. The IOP was respectively adjusted to 30, 45, 60 and 75 mmHg in these groups immediately after cannulation and was maintained throughout the experiment. An ultrasonic pachymeter was also applied every 10 minutes in the same manner as for groups T and C15.

## 4. Statistical analyses

Statistical analysis was performed using PASW Statistics 18 for Windows (SPSS Inc., Chicago, IL, USA). CCT data was expressed as the mean ± SE (standard error), and the level of significance used was $p < 0.05$. In one-way repeated measures ANOVA following pairwise comparison, Bonferroni adjustment was performed to evaluate the variation in CCT values against time in the same group and to evaluate variation in the difference in CCT (dCCT) from baseline (10 minutes after cannulation) against time, which was compared with dCCT at the same time point between groups.

## Results

There was a significant difference in the effect of time on CCT ($p < 0.001$) between groups. There was no significant difference in the effect of time on CCT in group C15 ($p=0.729$). The CCT in group C15 remained constant over the course of 70 minutes. However, there was a significant difference in the effect of time on CCT in group T ($p<0.001$). The CCT in group T initially decreased until 40 minutes and then began to increase. The CCT in group T was unchanged at 20 minutes compared with at 10 minutes. However, the CCTs at 30 ($p=0.006$) and 40 minutes ($p=0.028$) were significantly thinner than that at 10 minutes in group T. Furthermore, the CCTs at 50, 60 and 70 minutes were significantly thicker than those at 30 and 40 minutes in group T. There was a significant difference in the effect of time on CCT in group C30 ($p=0.032$). The CCT in group C30 decreased until 30 minutes and was then maintained. The CCT in group C30 was unchanged at 20 minutes compared with at 10 minutes. However, the CCTs at 30 ($p=0.003$) and 40 minutes ($p=0.045$) were significantly thinner than that at 10 minutes in group C30. There was a significant difference in the effect of time on CCT in group C45 ($p < 0.001$). The CCT in group C45 was unchanged at 40 minutes compared with at 10 minutes and then showed a significant increase. The CCTs in group C45 at 20, 30 and 40 minutes were significantly thinner than those at 50, 60 and 70 minutes. There was a significant difference in the effect of time on CCT in group C60 ($p < 0.001$) and group C75 ($p < 0.001$). The CCT in group C60 was unchanged at 20 minutes compared with at 10 minutes and then showed a significant increase, except at 50 minutes to 60 minutes. The CCT in group C75

showed a steady significant increase after cannulation, except at 30 minutes to 40 minutes.

There was a significant difference in the effect of time on dCCT ($p < 0.001$) between groups. There was a statistically significant difference in dCCT between groups C15 and C70 at 20 minutes ($p=0.040$). The dCCTs in groups C60 ($p=0.031$) and C75 ($p=0.001$) were significantly thicker than that in group C30 at 20 minutes. The dCCTs in groups C60 and C75 were also significantly thicker than those in groups T, C15, C30 and C45 at 30, 40, 50, 60 and 70 minutes. There was a statistically significant difference in dCCT between groups C15 and C30 at 30 minutes ($p=0.010$). There were also statistically significant differences in dCCT between groups T and C30 at 60 ($p=0.012$) and 70 minutes ($p=0.016$). There were statistically significant differences in dCCT between groups C30 and C45 at 50 ($p=0.024$), 60 ($p=0.008$) and 70 minutes ($p=0.005$).

Table 2. Central corneal thickness (CCT; microns) changes according to experimental adjustment of intraocular pressure (IOP).

| The time after cannulation (minute) | IOP of T group (mmHg) | T | C15* | C30* | C45* | C60* | C75* |
|---|---|---|---|---|---|---|---|
| 10 | 10 | 519.8 ± 15.0 | 513.9 ± 15.0 | 508.1 ± 23.3 | 487.7 ± 23.3 | 513.3± 23.3 | 480.2 ± 23.3 |
| 20 | 20 | 516.3 ± 15.1 | 513.6 ± 15.1 | 500.4 ±23.1 | 479.5 ± 23.1 | 519.4 ±23.1 | 490.8± 23.1[a)] |
| 30 | 30 | 512.2 ± 14.9[a)] | 514.2 ± 14.9 | 494.2 ± 22.9[a)] | 482.5 ± 22.9 | 531.5± 22.9[a),b)] | 504.7 ± 22.9[a),b)] |
| 40 | 40 | 511.7 ± 15.1[a)] | 513.9 ± 15.1 | 494.7 ± 23.0[a)] | 486.8 ± 23.0 | 544.9 ±23.0[a),b),c)] | 512.2 ± 23.0[a),b)] |
| 50 | 50 | 519.1 ± 15.6[c),d)] | 513.6 ± 15.6 | 494.3 ± 23.4 | 498.5 ± 23.4[b),c),d)] | 557.3± 23.4 [a),b),c),d)] | 524.1 ± 23.4 [a),b),c),d)] |
| 60 | 60 | 529.8 ± 15.4 [b),c),d),e)] | 512.3 ± 15.4 | 494.3 ± 23.4 | 504.1 ± 23.4[b),c),d)] | 561.9± 23.4 [a),b),c),d)] | 532.7 ± 23.4 [a),b),c),d),e)] |
| 70 | 70 | 535.3 ± 15.2 [a),b),c),d),e)] | 515.3 ± 15.2 | 495.3 ± 23.4 | 513.3 ± 23.4 [a),b),c),d),e)] | 581.1± 23.4 [a),b),c),d),e),f)] | 545.5 ± 23.4 [a),b),c),d),e),f)] |

Data for CCT are expressed as the mean ± SE (standard error); [a)]Values in the same column with this superscript are significantly different ($p<0.05$) compared with the CCT at 10 minutes; [b)]Values in the same column with this superscript are significantly different ($p<0.05$) compared with the CCT at 20 minutes from 30 minutes onward; [c)]Values in the same column with this superscript are significantly different ($p<0.05$) compared with the CCT at 30 minutes from 40 minutes onward; [d)]Values in the same column with this superscript are significantly different ($p<0.05$) compared with the CCT at 40 minutes from 50 minutes onward; [e)]Values in the same column with this superscript are significantly different ($p<0.05$) compared with the CCT at 50 minutes from 60 minutes onward; [f)]Values in the same column with this superscript are significantly different ($p<0.05$) in CCT at 70 minutes compared with that at 60 minutes; * The IOPs of groups C15, C30, C45, C60 and C 75 were maintained at 15, 30, 45, 60 and 75 mmHg, respectively, during the experiment.

Table 3. Difference in CCT (dCCT; microns) from baseline value according to experimental adjustment of intraocular pressure (IOP).

| The time after cannulation (minute) | IOP of T group (mmHg) | T | C15* | C30* | C45* | C60* | C75* |
|---|---|---|---|---|---|---|---|
| 10 (baseline) | 10 | 0 | 0 | 0 | 0 | 0 | 0 |
| 20 | 20 | -3.5 ± 1.7[f)] | -0.3 ± 1.7[f)] | -7.7 ± 3.0[e),f)] | -8.2 ± 3.0[e),f)] | 6.1 ± 3.0[c),d)] | 10.6 ± 3.0[a),b),c),d)] |
| 30 | 30 | -7.6 ± 1.9[e),f)] | 0.3 ± 1.9[c),e),f)] | -13.9 ± 3.4[b),e),f)] | -5.1 ± 3.4[e),f)] | 18.1 ± 3.4[a),b),c),d)] | 24.4 ± 3.4[a),b),c),d)] |
| 40 | 40 | -8.1 ± 2.4[e),f)] | 0.0 ± 2.4[e),f)] | -13.4 ± 4.1[e),f)] | -0.9 ± 4.1[e),f)] | 31.5 ± 4.1[a),b),c),d)] | 32.0 ± 4.1[a),b),c),d)] |
| 50 | 50 | -0.7 ± 3.0[e),f)] | -0.3 ± 3.0[e),f)] | -13.8 ± 5.1[d),e),f)] | 10.8 ± 5.2[c),e),f)] | 44.0 ± 5.2[a),b),c),d)] | 43.8 ± 5.2[a),b),c),d)] |
| 60 | 60 | 10.0 ± 3.3[c),e),f)] | -1.5 ± 3.3[e),f)] | -13.8 ± 5.7[a),d),e),f)] | 16.4 ± 5.7[c),e),f)] | 48.6 ± 5.7[a),b),c),d)] | 52.5 ± 5.7[a),b),c),d)] |
| 70 | 70 | 15.5 ± 4.0[e),f)] | 1.4 ± 4.0[e),f)] | -12.9 ± 7.0[a),d),e),f)] | 25.6 ± 7.0[c),e),f)] | 67.7 ± 7.0[a),b),c),d)] | 65.2 ± 7.0[a),b),c),d)] |

Data for dCCT are expressed as the mean ± SE (standard error); [a)]Values in the same row with this superscript are significantly different ($p<0.05$) compared with the group T; [b)]Values in the same row with this superscript are significantly different ($p<0.05$) compared with the group C15; [c)]Values in the same row with this superscript are significantly different ($p<0.05$) compared with the group C30; [d)]Values in the same row with this superscript are significantly different ($p<0.05$) compared with the group C45; [e)]Values in the same row with this superscript are significantly different ($p<0.05$) compared with the group C60; [f)]Values in the same row with this superscript are significantly different ($p<0.05$) compared with the group C75; [*]The IOPs of groups C15, C30, C45, C60 and C75 were maintained at 15, 30, 45, 60 and 75 mmHg, respectively, during the experiment.

## Discussion

Although IOP can be a factor in CCT variation, there are few experimental studies that have investigated this relationship in either animals or humans (Lam and Douthwaite, 1997; Ytteborg and Dohlman, 1965a). The current study showed that CCT varied according to different experimental adjustments of IOP. The CCT showed two core changes according to increased IOP. CCT initially decreased in response to increased IOP in groups T and C30. Also, a significant decrease in dCCT in group C30 compared with C15 was identified at 30 minutes. However, in groups T, C45, C60 and C75, it appears that the CCT ultimately increased after passing the critical pressure. Comparing groups C45, C60 and C75, there is evidence to say the duration and degree of increase in IOP was a factor contributing to the increase in CCT.

In previous human studies, there was no obvious change in CCT when the IOP was increased by approximately 10 mmHg, although the duration of the increase in IOP was only 5 minutes (Lam and Douthwaite, 1997). A similar result was found in the current study, with no statistical difference in CCT values between 10 and 20 mmHg in group T. However, a significant difference in CCT was shown in this group when the IOP was elevated above 30 mmHg, which is adjacent to the upper limit of the physiologically normal IOP (Gelatt and MacKay, 1998).

Olsen (1980) suggested that IOP showed a dual effect on corneal thickness according to corneal endothelium conditions in human patients with acute glaucoma. First, CCT decreases in response to an increase in IOP in the intact corneal endothelium, and second, it increases in the acutely damaged corneal endothelium. Ehlers and Riise (1967) documented that CCT in eyes with a low IOP was thicker than that in contralateral normal

eyes in human patients with retinal detachment. The results of this study also indicated a similar conclusion. Initially, CCT gradually decreased with an increase in IOP until 40 minutes (40 mmHg) in group T. The CCTs at 30 and 40 minutes were significantly different from that at 10 minutes in group T. However, CCT was increased from 50 minutes (50 mmHg) to 70 minutes (70 mmHg) in group T. The CCTs at 30 and 40 minutes were significantly different from those at 50, 60 and 70 minutes in group T.

The initial decrease in CCT according to elevated IOP is associated with microsturctural changes in the corneal anterior stroma. The anterior stroma is more resistant to corneal hydration, and the transverse collagen lamellae of the anterior stroma are short (Bron, 2001; Wu and Yeh, 2008). An initial decrease in CCT can be caused by immediate loss of anterior stromal interlamellar gaps with increasing IOP in rabbits (Wu and Yeh, 2008).

Abnormal thickening of the cornea presents as corneal edema, which can appear when the IOP is above 40 mmHg in human glaucoma patients (Ytteborg and Dohlman, 1965b). In this study, CCT increased after IOP passed the lowest point of 40 mmHg (40 minutes) in group T, and significant differences in CCT were also observed between CCTs in group C45 at 20 minutes and 50 minutes. Therefore, it can be proposed that corneal endothelial decompensation was initiated at an IOP of 40 to 45 mmHg in normal canine eyes. The duration and degree of increased IOP should also be considered when assessing the initiation of thickening of the CCT. In group C45, there was a significant increase in CCT beginning at 50 minutes. Also, there were significant increases in CCT beginning at 30 minutes and 20 minutes in groups C60 and C75, respectively. Furthermore, there were significant increases in dCCT compared with group C15 beginning at 30 minutes and 20 minutes in groups C60 and C75, respectively. Therefore, the initiation of thickening of the

CCT was influenced by the duration and degree of IOP increase. A high degree of IOP may cause thickening of the CCT to occur rapidly.

In humans, a thin CCT was considered a risk factor for glaucoma in the Ocular Hypertension Treatment Study (Gordon *et al.*, 2002). This relationship might be partially explained when considering the effect of CCT on IOP measurement (Manni *et al.*, 2008). Although the effect of CCT was different with each type of tonometer used, the measured IOP can be lower than the real IOP in both humans and dogs with a thin CCT (Bhan *et al.*, 2002; Iliev *et al.*, 2006; Park *et al.*, 2011). Therefore, glaucoma patients with a thin CCT can be measured as having a normal IOP when using tonometry. CCT is also correlated with the development of glaucomatous visual field loss in humans (Gunvant *et al.*, 2008; Lin *et al.*, 2009; Medeiros *et al.*, 2003). Although this study was performed over a short duration (70 minutes), the results support that thin CCT can be a promising source for diagnosis and monitoring of glaucoma in dogs. Thinning of the cornea was not correlated with tonometer readings in this study, because manometric values were used. Although the reductions in CCT were quite small, there were significant differences in CCT between 10 minutes and 30 minutes in groups T and C30. CCT itself changed with an increased IOP, exhibiting an initial decrease and then a subsequent increase.

## Conclusions

In this study, changes in CCT according to experimental adjustment of IOP were documented, and the possibility of using CCT as a diagnostic and monitoring factor for canine glaucoma was suggested. This study provides basic data to enable further investigation of the relationship between CCT and IOP in dogs.

# GENERAL CONCLUSIONS

This study was designed to investigate possibility of CCT as a diagnosis and monitoring of canine glaucoma.

In chapter I, the effect of CCT on IOP values obtained by two different tonometers (the TonoPen XL and the TonoVet) were investigated in normal dogs. The IOP values measured by the tonometers tended to be elevated as the CCT increased. However, the degree of dependency on the CCT was more prominent in the rebound tonometer (TonoVet) than the applanation tonometer (TonoPen XL) in dogs. Every 100 microns increase in CCT, there was an elevation of 1 and 2 mmHg in IOP measured by the TonoPen XL and TonoVet, respectively. Also, despite the correlation between the two tonometric values, IOP measurements obtained by the TonoPen XL were also significantly lower than those of the TonoVet (on average, 5.3 mmHg) in normal beagle dogs.

In chapter II, acute changes in CCT according to experimental adjustment of IOP were investigated in normal dogs. The CCT showed two core changes according to increased IOP. CCT initially decreased in response to increased IOP and it ultimately increased after passing the critical pressure. Also, the initiation of thickening of the CCT was influenced by the duration and degree of IOP increase. A high degree of IOP may cause thickening of the CCT to occur rapidly.

Through these studies, it is demonstrated that CCT can be a promising source of glaucoma monitoring and diagnosis. Especially, dogs with thin cornea have a high risk for glaucoma in dogs.

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# 국 문 초 록

# 개의 녹내장 진단 시 중심각막두께의 적용

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녹내장은 개에서 시력 소실을 일으키는 원인 중 두 번째로 흔한 질환이다. 개와 사람에서 안압 상승으로 인한 망막신경절세포의 손상은 영구적인 실명을 유발한다. 녹내장에 이환된 환자가 오래 동안 시력을 유지하기 위해서는 이 질환을 조기에 발견하여 정기적으로 모니터링하는 것이 중요하다. 현재까지 개에서 녹내장의 진단과 모니터링은 안압계를 통한 안압 측정에만 의존하고 있는 실정이다. 초음파 각막두께 측정계 (ultrasonic pachymeter) 가 사용되기 시작하면서 사람에서는 중심각막두께 (CCT) 와 녹내장의 연관성에 대한 연구가 활발하게 진행되어오고 있다. Ocular Hypertension Treatment Study 에 의하면 고안압인 환자가 녹내장으로 진행될 가능성을 예측하는데

중심각막두께 가 가장 영향력이 있는 예측 인자로 확인되었다. 개에서 중심 및 변연부 각막 두께를 측정한 논문은 있지만, 중심각막두께와 녹내장의 연관성에 대한 연구는 거의 없는 실정이다. 본 연구는 중심각막두께를 개의 녹내장 진단 및 모니터링에 이용할 수 있는지 알아보기 위해 실시되었다. 본 논문은 총 2개의 장으로 구성되어 있다.

제1장에서는 안압계를 통한 안압 측정에 중심각막두께가 미치는 영향을 연구하였다. 본 연구에는 정상 비글견 60두의 양쪽 눈을 모두 이용하였다. 절반의 개에서는 안압을 TonoVet 으로 먼저 측정한 후 TonoPen XL 로 측정하였으며 나머지 절반은 순서를 반대로 하여 측정하였다. 중심각막두께 측정은 마지막 안압 측정 10분 후에 실시하였다. 회귀분석에서 두 가지 안압계로 측정한 안압과 중심각막두께 사이에는 연관성이 확인되었다 (TonoVet: $p=0.002$, TonoPen XL: $p=0.035$). 산출된 회귀 방정식에서 중심각막두께가 100 ㎛ 증가할 때마다 TonoPen XL 과 TonoVet 으로 측정된 안압은 각각 1 과 2 mmHg씩 증가되었다.

제2장에서는 안압을 실험적으로 조정하면서 중심각막두께의 변화를 관찰하였다. 정상 비글견 25두의 양쪽 눈을 모두 이용하였다. 안압을 조정하고 측정하기 위해서 두 개의 26 gauge 바늘을 각각의 눈에 삽입하였다. 한 개의 바늘은 압력계에 연결하였으며, 다른 한 개의 바늘은 높이를 조절할 수 있는 스탠드에 걸린 생리식염수에 연결하였다. 실험군 (Group T)에서 안압은 10 mmHg 부터 70 mmHg 까지 10mmHg 단위로 단계적으로 증가시켰다. 또한 5개의 대조군에서는 실험하는 동안 안압은 각각 15 mmHg

(대조군 15, Group C15), 30 mmHg (대조군 30, Group C30), 45 mmHg (대조군 45, Group C45), 60 mmHg (대조군 60, Group C60), 75 mmHg (대조군 75, Group C75) 로 일정하게 유지하였다. 중심각막두께는 초음파 각막두께 측정계를 이용하여 측정하였으며, 바늘을 삽입한 후 매 10분마다 측정하였다. 안압 상승에 따라 중심각막두께는 처음에는 감소하는 반응을 보이다가 다시 상승하는 양상을 보였다.

본 연구의 결과에 따르면 개에서 안압계로 측정된 안압은 중심각막두께의 영향을 받는다. 또한, 중심각막두께는 안압이 점차 증가됨에 따라 초기에 감소하다가 다시 증가하는 양상을 보인다. 중심각막두께는 개에서 녹내장 진단과 모니터링에 유용하게 이용될 수 있을 것으로 판단된다.

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